Aroga:
CANCER & FOOD

Dr. BILL MCANALLEY Ph.D.
AROGA President
Co-Founder & Chief Science Officer

Dr McAnalley leads Arogas cutting-edge research product development.

His passion as a scientist is his focus on developing proprietary natural products that help build health and he currently holds 300+ patents.

Increased Bcl-2 expression allows cancer:

"Bcl-2 and cancer"

Mol Ther Nucleic Acids
2013 Sep 10;2(9):e121. doi: 10.1038/mtna.2013.45. PMID: 24022053

Therapeutic Silencing of Bcl-2 by Systemically Administered siRNA Nanotherapeutics Inhibits Tumor Growth by Autophagy and Apoptosis and Enhances the Efficacy of Chemotherapy in Orthotopic Xenograft Models of ER (-) and ER (+) Breast Cancer

Ibrahim Tekedereli 1 , S Neslihan Alpay, Ugur Akar, Erkan Yuca, Cristian Ayugo- Rodriguez, He-Dong Han, Anil K Sood, Gabriel Lopez-Berestein, Bulent Ozpolat

Affiliation
1) Department of Experimental Therapeutics,
The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, Texas 77030, USA.

Abstract

Bcl-2 is overexpressed in about a half of human cancers and 50-70% of breast cancer patients, thereby conferring resistance to conventional therapies and making it an excellent therapeutic target.

Small interfering RNA (siRNA) offers novel and powerful tools for specific gene silencing and molecularly targeted therapy.

Here, we show that therapeutic silencing of Bcl-2 by systemically administered nanoliposomal (NL)-Bcl-2 siRNA (0.15 mg siRNA/ kg, intravenous) twice a week leads to significant antitumor activity and suppression of growth in both estrogen receptor-negative (ER(-)) MDA-MB-231 and ER-positive (+) MCF7 breast tumors in orthotopic xenograft models ($P < 0.05$).

A single intravenous injection of NL-Bcl-2-siRNA provided robust and persistent silencing of the target gene expression in xenograft tumors. NL-Bcl-2- siRNA treatment significantly increased the efficacy of chemotherapy when combined with doxorubicin in both MDA-MB-231 and MCF-7 animal models ($P < 0.05$). NL-Bcl-2-siRNA treatment-induced apoptosis and autophagic cell death, and inhibited cyclin D1, HIF1α and Src/Fak signaling in tumors.

In conclusion, our data provide the first evidence that in vivo therapeutic targeting Bcl-2 by systemically administered nanoliposomal-siRNA significantly inhibits growth of both ER(-) and ER(+) breast tumors…

…and enhances the efficacy of chemotherapy, suggesting that therapeutic silencing of Bcl-2 by siRNA is a viable approach in breast cancers.

Molecular Therapy- Nucleic Acids (2013) 2, e121; doi:10.1038/mtna.2013.45; published online 10 September 2013.
cogene. 2000 Nov 2;19(46):5251-8.

Bcl-2 accelerates multistep prostate carcinogenesis in vivo

E M Bruckheimer 1, S Brisbay, D J Johnson, J R Gingrich, N Greenberg, T J McDonnell

Affiliation

1) Department of Molecular Pathology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas, TX 77030, USA.
PMID: 11077442 DOI: 10.1038/sj.onc.1203881

Abstract

The impact of bcl-2 proto-oncogene expression on the pathogenesis and progression of prostate cancer was examined in a transgenic mouse model. Probasin-bcl-2 transgenic mice were crossed with TRAMP (TRansgenic Adenocarcinoma Mouse Prostate) mice that express the SV40 early genes (T/t antigens) under probasin control.

Prostate size, cell proliferation, apoptosis, and the incidence and latency of tumor formation were evaluated.

The double transgenic, probasin-bcl-2 X TRAMP F1 (BxT) mice exhibited an increase in the wet weight of the prostate.

This was associated with an increase in proliferation, attributable to T/t antigens, and a decrease in apoptosis attributable to bcl-2.

The latency to tumor formation was also decreased in the BxT mice compared to the TRAMP mice.

The incidence of metastases was identical in both the TRAMP and BxT mice.

Lastly, the incidence of hormone-independent prostate cancer was reduced in the BxT mice compared to the TRAMP mice.

Together, these results demonstrate that bcl-2 can facilitate multistep prostate carcinogenesis in vivo.

How can Bcl-2 be easily lowered?

Mol Pharmacol . 1998 Mar;53(3):415-21. doi: 10.1124/mol.53.3.415.

Induction of apoptosis in a macrophage cell line RAW 264.7 by acemannan, a beta-(1,4)-acetylated mannan

L Ramamoorthy 1, I R Tizard

Affiliation

1) Department of Veterinary Pathobiology, Texas A & M University, College Station, Texas 77843, USA. l0r7859@nigel.tamu.edu
PMID: 9495806 DOI: 10.1124/mol.53.3.415

Abstract

Acemannan is a polydispersed beta-(1,4)-linked acetylated mannan with antiviral properties. It is an immunomodulator, and studies in our laboratory have shown that it causes activation of macrophages.

In the presence of IFNgamma, acemannan induced apoptosis in RAW 264. 7 cells. These cells exhibited chromatin condensation, DNA fragmentation, and laddering characteristic of apoptosis.

The induction of apoptosis by acemannan and IFNgamma does not seem to be mediated by nitric oxide, since N-nitro-L-arginine methyl ester, the nitric oxide inhibitor, had no effect.

Acemannan in the presence of IFNgamma also inhibited the expression of bcl-2.

These results suggest that acemannan in the presence of IFNgamma induces apoptosis in RAW 264.7 cells through a mechanism involving the inhibition of bcl-2 expression.

Several isoflavones, flavonoids, lignans, phytosterols intake stop prostate cancer:

Nutr Cancer . 1999;33(1):20-5. doi: 10.1080/01635589909514743.

Phytoestrogen intake and prostate cancer: a case-control study using a new database

S S Strom 1, Y Yamamura, C M Duphorne, M R Spitz, R J Babaian, P C Pillow, S D Hursting

Affiliation: 1) Department of Epidemiology, University of Texas M. D. Anderson Cancer Center, Houston 77030, USA.

PMID: 10227039 DOI: 10.1080/01635589909514743

Erratum in: Nutr Cancer 2000;36(2):243

Abstract

In the last several years, attention has been focused on comparing the Western diet, which is rich in fat, protein, and refined carbohydrates, with the Asian diet, which is rich in phytoestrogens, as a possible explanation for the contrasting rates of clinically relevant prostate cancer.

Phytoestrogens, plant-derived nutrients, include several isoflavones, flavonoids, lignans, phytosterols, and coumestans, some of which have been postulated as having anticarcinogenic properties.

Using a new database, we examined the role of phytoestrogen intake and prostate cancer risk in 83 Caucasian cases and 107 controls.

Controls reported consuming higher amounts of **foods containing genistein, daidzein, and coumestrol, and lower amounts of foods containing campesterol and stigmasterol**.

Multivariate analysis, after adjustment for age, family history of prostate cancer, alcohol consumption, and total calorie intake, showed an inverse association between coumestrol (p = 0.03) and daidzein (p = 0.07) and prostate cancer risk.

Genistein, the most studied phytoestrogen, showed a slight protective effect (p = 0.26). However, a positive association was found between campesterol (p = 0.08) and stigmasterol (p = 0.03) and risk of prostate cancer.

These results suggest a possible relationship between phytoestrogen intake & prostate cancer risk. Larger comprehensive studies are needed to further refine the role of phytoestrogen intake in prostate cancer risk.

Dietary agents for prevention and therapy for cancer:

Review: Biochem Pharmacol

2006 May 14;71(10):1397-421. doi: 10.1016/j.bcp.2006.02.009. Epub 2006 Feb 23.

Molecular targets of dietary agents for prevention & therapy of cancer

Bharat B Aggarwal 1, Shishir Shishodia

Affiliation 1) Cytokine Research Laboratory, Department of Experimental Therapeutics, The University of Texas M.D. Anderson Cancer Center, Box 143, 1515 Holcombe Boulevard, Houston, TX 77030, USA.
aggarwal@mdanderson.org

PMID: 16563357 DOI: 10.1016/j.bcp.2006.02.009

Abstract

While fruits and vegetables are recommended for prevention of cancer and other diseases, their active ingredients (at the molecular level) and their mechanisms of action less well understood.

Extensive research during the last half century has identified various molecular targets that can potentially be used not only for the prevention of cancer but also for treatment.
However, lack of success with targeted monotherapy resulting from bypass mechanisms has forced researchers to employ either combination therapy or agents that interfere with multiple cell-signaling pathways.

In this review, we present evidence that numerous agents identified from fruits and vegetables can interfere with several cell-signaling pathways.

The agents include

Curcumin (turmeric)
Resveratrol (red grapes, peanuts & berries)
Genistein (soybean)
S-allyl cysteine (allium)
Lycopene (tomato)
Diosgenin (fenugreek)
Ellagic acid (pomegranate)
Catechins (green tea)
Limonene (citrus fruits)
Diallyl sulfide (allium)
Allicin (garlic)
Capsaicin (red chilli)
6-gingerol (ginger),
Silymarin (milk thistle)
Eugenol (cloves)
Beta carotene (carrots),
Anethol (anise, camphor, and fennel)
Ursolic acid (apple, pears, prunes)
Indole-3-carbinol (cruciferous vegetables),
& Dietary fiber.

For instance, the cell-signaling pathways inhibited by curcumin alone include NF-kappaB, AP-1, STAT3, Akt, Bcl-2, Bcl-X(L), caspases, PARP, IKK, EGFR, HER2, JNK, MAPK, COX2, and 5-LOX.

The active principle identified in fruit and vegetables and the molecular targets modulated may be the basis for how these dietary agents not only prevent but also treat cancer and other diseases.

This work reaffirms what Hippocrates said 25 centuries ago:

"Let food be thy medicine and medicine be thy food"

Review Expert Opin Investig Drugs . 2004 Oct;13(10):1327-38.

From chemoprevention to chemotherapy: common targets and common goals

Bharat B Aggarwal 1, Yasunari Takada, Oommen V Oommen

Affiliation

1) The University of Texas M.D. Anderson Cancer Center, Cytokine Research Section, Department of Experimental Therapeutics, PO Box 143, 1515 Holcombe Boulevard, Houston, Texas 77030, USA. aggarwal@mdanderson.org

PMID: 15461561 DOI: 10.1517/13543784.13.10.1327

Abstract

Three decades of research have revealed that cancer is easier to prevent than to treat and that consumption of certain fruits and vegetables can reduce the risk of cancer.

Whereas chemotherapy is designed to destroy cancer after it appears, chemoprevention involves the abrogation or delay in the onset of cancer.

Regardless of whether a chemopreventive or chemotherapeutic approach is taken, cancer is a multifactorial disease that requires modulation of multiple pathways and multiple targets.

Various molecular targets of chemoprevention are also relevant to the therapy of cancer.

These targets include the activation of apoptosis; suppression of growth factor expression or signalling; downregulation of antiapoptotic proteins; suppression of phosphatidylinositol-3'-kinase/Akt, NF-kappaB, Janus kinase-signal transducer and activator of transcription and activator protein-1 signalling pathways; and downregulation of angiogenesis through inhibition of vascular endothelial growth factor expression,

cyclooxygenase-2, matrix metalloproteinase-9, urokinase-type plasminogen activator, adhesion molecules and cyclin D1. Pharmacologically safe phytochemicals that have been identified from plants or their variant forms can modulate these molecular targets.

These phytochemicals include genistein, resveratrol, dially sulfide, S-ally cysteine, allicin, lycopene, capsaicin, curcumin, 6-gingerol, ellagic acid, ursolic acid, betulinic acid, flavopiridol, silymarin, anethol, catechins and eugenol. Recent work has shown that these phytochemicals also can reverse chemoresistance and radioresistance.

Because of their pharmacological safety, these agents can be used alone to prevent cancer and in combination with chemotherapy to treat cancer.

Review
Anticancer Res. Jan-Feb 2003;23(1A):363-98.

Anticancer potential of curcumin: preclinical and clinical studies

Bharat B Aggarwal 1, Anushree Kumar, Alok C Bharti

Affiliation

1) Cytokine Research Section, Department of Bioimmunotherapy, University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Boulevard, Box 143, Houston, TX, USA. aggarwal@mdanderson.org

PMID: 12680238

Abstract

Curcumin (diferuloylmethane) is a polyphenol derived from the plant Curcuma longa, commonly called turmeric. Extensive research over the last 50 years has indicated this polyphenol can both prevent and treat cancer.

The anticancer potential of curcumin stems from its ability to suppress proliferation of a wide variety of tumor cells, down-regulate transcription factors NF-kappa B, AP-1 and Egr-1; down-regulate the expression of COX2, LOX, NOS, MMP-9, uPA, TNF, chemokines, cell surface adhesion molecules and cyclin D1; down-regulate growth factor receptors (such as EGFR and HER2); and inhibit the activity of c-Jun N-terminal kinase, protein tyrosine kinases and protein serine/threonine kinases.

In several systems, curcumin has been described as a potent antioxidant and anti-inflammatory agent.

Evidence has also been presented to suggest that curcumin can suppress tumor initiation, promotion and metastasis. Pharmacologically, curcumin has been found to be safe. Human clinical trials indicated no dose-limiting toxicity when administered at doses up to 10 g/day.

All of these studies suggest that curcumin has enormous potential in the prevention and therapy of cancer.

The current review describes in detail the data supporting these studies

Review
Antioxid Redox Signal. Nov-Dec 2005;7(11-12):1630-47. doi: 10.1089/ars.2005.7.1630.

Chemosensitization and radiosensitization of tumors by plant polyphenols

Amit K Garg 1, Thomas A Buchholz, Bharat B Aggarwal
Affiliation
1) Department of Radiation Oncology, University of Texas M.D. Anderson Cancer Center, Houston, TX 77030, USA.
PMID: 16356126 DOI: 10.1089/ars.2005.7.1630

Abstract

The treatment of cancer with chemotherapeutic agents and radiation has two major problems: time-dependent development of tumor resistance to therapy (chemoresistance and radioresistance) and nonspecific toxicity toward normal cells.

Many plant-derived polyphenols have been studied intently for their potential chemopreventive properties and are pharmacologically safe.

These compounds include genistein, curcumin, resveratrol, silymarin, caffeic acid phenethyl ester, flavopiridol, emodin, green tea polyphenols, piperine, oleandrin, ursolic acid, and betulinic acid.

Recent research has suggested that these plant polyphenols might be used to sensitize tumor cells to chemotherapeutic agents and radiation therapy by inhibiting pathways that lead to treatment resistance.

These agents have also been found to be protective from therapy-associated toxicities. How these polyphenols protect normal cells and sensitize tumor cells to treatment is discussed in this review.
Antioxid. Redox Signal. 7, 1630-1647.

Foods can reduce reoccurrence of cancer caused by Cancer stem cells:

Review
Semin Oncol. 2015 Apr;42 Suppl 1:S3-17. Epub 2015 Jan 21.

Cancer stem cells: the promise and the potential

Jaffer A Ajani 1, Shumei Song 2, Howard S Hochster 3, Ira B Steinberg 4
Affiliations
1) Professor, Department of Gastrointestinal (GI) Medical Oncology, Division of Cancer Medicine; Professor, Department of Epidemiology, Division of OVP, Cancer Prevention and Population Sciences, The University of Texas MD Anderson Cancer Center, Houston, TX. Electronic address: Jajani@mdanderson.org.
2) Associate Professor, Department of Gastrointestinal (GI) Medical Oncology-Research, Division of Cancer Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX.
3) Assoc.Director, Yale Cancer Center; Professor of Medicine, Yale School of Medicine, New Haven, CT.
4) Vice President, Medical Affairs, Boston Biomedical, Cambridge, MA.
PMID: 25839664 DOI: 10.1053/j.seminoncol.2015.01.001

Abstract

Despite the advancement of treatment modalities, many cancer patients experience tumor recurrence and metastasis at regional or distant sites. Evolving understanding of tumor biology has led to the hypothesis that tumors may possess a stem cell-like subpopulation known as cancer stem cells (CSCs) that may be involved in driving tumor propagation and pathogenesis.

Like normal stem cells (NSCs), CSCs can be identified by markers such as CD133, CD44, and ALDH. CSCs have the ability to self-renew and differentiate into different tumor components through stemness pathways, such as Wnt, TGF-β, STAT, and Hippo-YAP/TAZ, among others.

In NSCs, stemness pathways are strictly regulated and control many important biologic processes, including embryogenesis and intestinal crypt cellular regulation.

In contrast, stemness pathways in CSCs are significantly dysregulated. Combining current drugs with the targeting of these stemness pathways may significantly improve patient prognosis.

The aim of this supplement is to update clinicians on the accumulated evidence characterizing the role of CSCs in tumor initiation, heterogeneity, therapy resistance, and recurrence and metastasis, and the potential for effectively treating patients.

Review
J Nutr Biochem. 2012 Jul;23(7):691-8.

Cancer stem cells: potential target for bioactive food components

Young S Kim [1], William Farrar, Nancy H Colburn, John A Milner
Affiliation
1) Nutritional Science Research Group,
Division of Cancer Prevention,
National Cancer Institute, Bethesda, MD 20892, USA. yk47s@nih.gov
PMID: 22704055 PMCID: PMC4518442 DOI: 10.1016/j.jnutbio.2012.03.002

Abstract

Cancer stem cells often have phenotypic and functional characteristics similar to normal stem cells including the properties of self-renewal and differentiation.

Recent findings suggest that uncontrolled self-renewal may explain cancer relapses and may represent a critical target for cancer prevention.

It is conceivable that the loss of regulatory molecules resulting from inappropriate consumption of specific foods and their constituents may foster the aberrant self-renewal of cancer stem cells.

In fact, increasing evidence points to the network delivering signals for self-renewal from extracellular compartments to the nucleus including changes in stem cell environments, inducible expression of microRNAs, hyperplastic nuclear chromatin structures, and the on/off of differentiation process as possible sites of action for bioactive food components.

Published by Elsevier Inc.

Diverse dietary constituents such as vitamins A and D, genistein, (-)-epigallocatechin-3-gallate (EGCG), sulforaphane, curcumin, piperine, theanine and choline have been shown to modify self-renewal properties of cancer stem cells.

The ability of these bioactive food components to influence the balance between proliferative and quiescent cells by regulating critical feedback molecules in the network including dickkopf 1 (DKK-1), secreted frizzled-related protein 2 (sFRP2), B cell-specific Moloney murine leukemia virus integration site 1 (Bmi-1) and cyclin-dependent kinase 6 (CDK6) may account for their biological response.

Overall, the response to food components does not appear to be tissue or organ specific, suggesting there may be common cellular mechanisms.

Unquestionably, additional studies are needed to clarify the physiological role of these dietary components in preventing the resistance of tumor cells to traditional drugs and cancer recurrence.

Isoflavones, flavonoids, lignans, phytosterols and phytoestrogens are small bitter molecules in food that modulates and balances Apoptosis Pathways.
Drugs usually cause an imbalance in a specific Apoptosis Pathway.

This causes other pathways to move up or down to neutralize the drug effect.
This is referred to as 'Cross-talk' resulting in resistance to the desired drug effect.

These small bitter molecules re-balance the Apoptosis Pathways, so drugs and radiation can have the desired effect, as described in many of the PubMed Articles above.

Unfortunately many doctors are so busy they do not have time to keep up with the latest science reviewed above, so share this with them.

AROGA provides these ingredients in freeze dried food supplements.

This work reaffirms what Hippocrates said 25 centuries ago:

"Let food be thy medicine and medicine be thy food"